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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/772,964	02/04/2004	Claudia Mattern	85946.8276	5308

20999 7590 09/29/2009

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EXAMINER	
SASAN, ARADHANA	
ART UNIT	PAPER NUMBER
1615	
MAIL DATE	DELIVERY MODE
09/29/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/772,964	MATTERN, CLAUDIA	
	Examiner	Art Unit	
	ARADHANA SASAN	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 July 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,10-13 and 20-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8, 10-13 and 20-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. The remarks, amendments, and Request for Continued Examination filed on 07/15/09 are acknowledged.

2. Claims 9 and 14-19 were cancelled. Claims 1, 5-6, 8, 10, 12, 20 and 21 were amended. New claims 22-24 were added.

3. Claims 1-8, 10-13 and 20-24 are included in the prosecution.

Continued Examination under 37 CFR 1.114

4. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 07/15/09 has been entered.

Response to Arguments

Rejection of claims 1-6, 8, 13, 15-17 and 20 under 35 USC § 103(a)

5. Applicant's arguments see Page 5, filed 07/15/09, regarding the rejection of claims 1-6, 8, 13, 15-17 and 20 under 35 USC § 103(a) as being unpatentable over Illum (US 5,863,554), in view of Ko et al. (Journal of Microencapsulation 1998) have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, new ground(s) of rejection follow.

Rejection of claim 7 under 35 USC § 103(a)

6. Applicant's arguments see Page 5, filed 07/15/09, regarding the rejection of claim 7 under 35 USC § 103(a) as being unpatentable over Illum (US 5,863,554), in view of Ko et al. (Journal of Microencapsulation 1998) and further in view of Patel et al. (US 6,248,363) have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, new ground(s) of rejection follow.

Rejection of claims 9-10, 12 and 18-19 under 35 USC § 103(a)

7. Applicant's arguments see Page 8, filed 07/15/09, regarding the rejection of claims 9-10, 12 and 18-19 under 35 USC § 103(a) as being unpatentable over Illum (US 5,863,554), in view of Ko et al. (Journal of Microencapsulation 1998) and further in view of Dondeti (International Journal of Pharmaceutics 1996) have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, new ground(s) of rejection follow.

Rejection of claim 11 under 35 USC § 103(a)

8. Applicant's arguments see Page 8, filed 07/15/09, regarding the rejection of claims 9-10, 12 and 18-19 under 35 USC § 103(a) as being unpatentable over Illum (US 5,863,554), in view of Ko et al. (Journal of Microencapsulation 1998) and further in view of Glass (US 5,897,894) have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, new ground(s) of rejection follow.

Rejection of claim 22 under 35 USC § 103(a)

9. Applicant's arguments see Page 8, filed 07/15/09, regarding the rejection of claim 22 under 35 USC § 103(a) as being unpatentable over Illum (US 5,863,554), in view of

Ko et al. (Journal of Microencapsulation 1998) and further in view of Bechgaard et al. (US 5,397,771) have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, new ground(s) of rejection follow.

Rejection of claims 1-8, 10-12, 15, 18-19 and 21 under nonstatutory obviousness type double patenting

10. Applicant's filing of the terminal disclaimer against Application No. 11/560,187 on 10/14/08 is acknowledged. Please note that the terminal disclaimer has not been approved. Until the approval of the terminal disclaimer, the nonstatutory obviousness type double patenting rejection of 05/05/08 will be maintained.

Request for Interview

Applicant's request for interview (Page 10, filed 07/15/09) is acknowledged. An office action on the merits follows, and an interview can be scheduled based on Applicant's requirements.

New grounds

11. New grounds of rejection follow.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 1-6, 8, 10, 12-13, and 20-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ko et al. (Journal of Microencapsulation 1998) in view of Whittle et al. (US 2002/0136752 A1) and further in view of Bechgaard et al. (US 5,397,771).

The claimed invention is a lipophilic formulation for nasal application comprising: a) at least one sexual hormone drug in an amount of between 0.5 to 6.0% by weight of the formulation; b) at least one lipophilic or partly lipophilic carrier, comprising at least one oil in an amount of between 85% and 95% by weight of the formulation; and c) a compound or a mixture of compounds having a surface tension decreasing activity in an amount effective for *in situ* generation of an emulsion upon contact of the formulation with water; and d) a viscosity regulating agent, wherein no water is added to the formulation.

Ko teaches emulsion formulations of testosterone for nasal delivery (Abstract). The formulation materials include vegetable oil and surfactants (Page 198, Materials). The formulations are prepared by emulsification of the oil phase (containing the lipophilic testosterone and soybean oil) with the aqueous phase (further containing a surfactant) (Page 199, Preparation of formulations).

Ko does not expressly teach emulsion formulations of testosterone without any water added to the formulation.

Whittle teaches a pharmaceutical formulation for use in the administration of a lipophilic medicament via a mucosal surface, the formulation comprising at least one lipophilic medicament and a matrix comprising at least one self emulsifying agent which when hydrated forms an emulsion containing the lipophilic medicament which is capable

of adhering reversibly to a mucosal surface and allowing controlled release of the medicament (Page 1, [0001] and [0009]). Whittle teaches that "lipophilic medicaments can be effectively brought into intimidate contact with the absorptive mucous membrane when they are formulated in a self-emulsifying matrix" (Page 1, [0010]). "The matrix may further comprise one or more viscolising agents (agents which increase viscosity)" (Page 1, [0011]). Self-emulsifying surfactants, viscolising agents with adhesive properties such as sugar alcohols are disclosed (Page 2, [0020]).

Bechgaard teaches that vehicles used for nasal administration of biologically active substances possess lipophilic properties (Col. 1, lines 40-48). The biologically active substances include testosterone (Col. 5, lines 39-40 and Col. 6, lines 43-44). The pharmaceutical preparation also comprises surfactants (Col. 7, lines 55-58). Hydrophobic (and lipophilic) agents including castor oil are disclosed (Col. 10, lines 64-66). An anhydrous vehicle used in the method of administering a biologically active substance is disclosed (Col. 34, claim 8, lines 39-40).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make an emulsion formulation of testosterone, as taught by Ko, combine it with the self-emulsifying formulation comprising a lipophilic medicament, as taught by Whittle, further combine it with the anhydrous composition for nasal delivery comprising oils and testosterone, as taught by Bechgaard, and produce the instant invention.

One of ordinary skill in the art would do this because preparing a composition suitable for nasal administration that is anhydrous and contains testosterone as the

active agent, castor oil as the lipophilic agent and surfactants was known in the art, as evidenced by Bechgaard. One of ordinary skill in the art would combine this known technique with the teachings of Ko and Whittle because Bechgaard teaches that an anhydrous formulation may be useful in chronic dosing (Col. 25, lines 67-68).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Regarding instant claims 1, 5, 8 and 20-22, which disclose the weight percentages of components (a), (b), (c) and (d), a person with ordinary skill in the art would find it obvious over the teachings of Ko, Whittle and Bechgaard, and would modify the percentages of the formulation based on the required dosage and desired release profile, and the recited percentages are obvious variants unless there is evidence of criticality or unexpected results.

Regarding instant claims 2-4, the oil would have been obvious over the castor oil taught by Bechgaard (Col. 10, lines 64-66).

Regarding instant claim 6, the lecithin would have been obvious over the lecithin taught by Whittle (Page 3, [0031]).

Regarding instant claims 10 and 12, the viscosity regulating agent would have been obvious over the viscolising agent (Page 1, [0011]) including beeswax (Page 4, [0050]), sugars and starches (Page 4, [0045], [0052]) taught by Whittle.

Regarding instant claim 13, the testosterone would have been obvious over the testosterone taught by Ko (Abstract).

Regarding claims 23-24, the limitation of the level of unbound sexual hormone drug that is constant over at least 10 hours would have been an obvious variant over the formulation taught by Ko with controlled release of testosterone. One of ordinary skill in the art would find it obvious to modify the release profile of the drug based on the desired length of time for drug release and would modify the composition to extend or enhance the release. The recited time range for drug release level would have been an obvious variant unless there is evidence of criticality or unexpected results.

14. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ko et al. (Journal of Microencapsulation 1998) in view of Whittle et al. (US 2002/0136752 A1) and further in view of Bechgaard et al. (US 5,397,771) and Patel et al. (US 6,248,363).

The teachings of Ko, Whittle and Bechgaard are stated above.

Ko, Whittle and Bechgaard do not expressly teach oleoyl macrogolglyceride as the surfactant.

Patel teaches that the bioavailability of drugs (Col. 6, line 49) can be improved by their invention, which includes macrogolglycerides as the surfactant (Col. 35, line 46, Col. 65, lines 50-53, claim 16).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make an emulsion formulation of testosterone, as taught by Ko, combine it with the self-emulsifying formulation comprising a lipophilic medicament, as

taught by Whittle, further combine it with the anhydrous composition for nasal delivery comprising oils and testosterone, as taught by Bechgaard, use the oleoyl macrogolglyceride taught by Patel, and produce the instant invention.

A person with ordinary skill in the art at the time the invention was made would have used a variety of macrogolglycerides for surfactants. These macrogolglycerides would include different fatty acid esters and oleoyl macrogolglyceride. The motivation to use these surfactants would be to allow the emulsification and improve the bioavailability of poorly soluble, lipophilic drugs

Regarding instant claim 7, the limitation of oleoyl macrogolglyceride would have been obvious over the oleoyl macrogolglyceride taught by Patel (Col. 35, line 46, Col. 65, lines 40-53, claim 16).

15. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ko et al. (Journal of Microencapsulation 1998) in view of Whittle et al. (US 2002/0136752 A1) and further in view of Bechgaard et al. (US 5,397,771) and Lacy et al. (US 5,645,856).

The teachings of Ko, Whittle and Bechgaard are stated above.

Ko, Whittle and Bechgaard do not expressly teach colloidal silicon dioxide as a viscosity regulating agent.

Lacy teaches ingredients such as thickeners/suspending agents including colloidal silicon dioxide that can be incorporated in oil-based drug delivery systems (Col. 13, lines 58-67).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make an emulsion formulation of testosterone, as taught by Ko, combine it with the self-emulsifying formulation comprising a lipophilic medicament, as taught by Whittle, and with the anhydrous composition for nasal delivery comprising oils and testosterone, as taught by Bechgaard, further use colloidal silicon dioxide as a thickener/suspending agent, as taught by Lacy, and produce the instant invention.

One of ordinary skill in the art would find it obvious to try various thickeners/suspending agents in emulsion formulations and would choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success. Please see MPEP 2141.

Regarding instant claim 11, the colloidal silicon dioxide would have been obvious over the colloidal silicon dioxide used as a thickener/suspending agent by Lacy (Col. 13, lines 58-67).

Double Patenting

16. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

17. Claims 1-8, 10-12, 15, 18-19 and 21 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 6-8, 10-12, 16, 18-21 and 24-25 of copending Application No. 11/560,187 ('187 hereinafter). Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claims and claims of '187 are drawn to a formulation for nasal application comprising at least one hormone drug, at least one lipophilic or partly lipophilic carrier and at least one compound having surface tension decreasing activity, an amount effective for *in situ* generation of an emulsion upon contact of the formulation with water. The difference is that component (b) of instant claim 1 recites the range of the lipophilic carrier as between 60% and 98% by weight of the formulation. It would be obvious to one of ordinary skill in the art to modify the percentage of the lipophilic carrier in the formulation for nasal application during the process of routine optimization. The recited percentage range would have been an obvious variant unless there is evidence of criticality or unexpected results.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

13. No claims are allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Aradhana Sasan/
Examiner, Art Unit 1615

/MP WOODWARD/
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